A New Iodonium Ylide-Based Three-Component Reaction Leading to 2-Spirosubstituted Dihydrofurans under Microwave Irradiation

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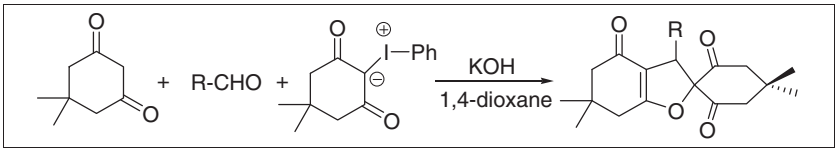

A new iodonium ylide-based three-component reaction for the synthesis of highly functionalized 2-spirosubstituted dihydrofurans starting from readily available common reactants has been developed under microwave irradiation. The procedure is facile, avoiding time-consuming and costly syntheses, tedious work-up and purifications of precursors as well as protection/deprotection of functional groups. This method is very efficient because of short reaction times and easy work-up and provides an efficient strategy for the construction of the polysubstituted spiro dihydrofuran skeleton.

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INTRODUCTION

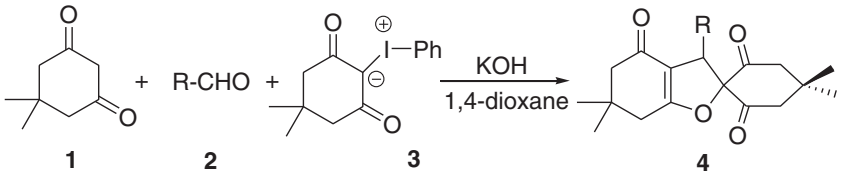
Substituted dihydrofurans occur frequently in numerous natural compounds, displaying significant biological activities and wide applications in pharmaceutical use [1]. For these reasons, the synthetic methodologies for dihydrofurans have fascinated to chemists for many years. A methodology to synthesize 2,3-dihydrofurans from the dehydration of 1,4-diols under high temperature and pressure conditions was presented by Dimroth and Pasedach in 1960 [2]. Then another way to generate 2,3-dihydrofuran moiety through intramolecular cyclization of alkynyl alcohols in the presence of a pentacarbonylmolybdenum/triethylamine complex was realized in 1993 [3]. The dihydrofuran moiety could also be constructed by Rh-catalyzed reactions of alkenes with diazo compounds or iodonium ylides [4]. More commonly, oxidative cyclization of alkenes with active methylene compounds promoted by metal salts, such as cerium(IV) ammonium nitrate and manganese(III) acetate, to the construct requisite dihydrofuran motif have been arousing wide concern [5]. However, these reported procedures often required severe reaction conditions or heavy metal catalysts. Therefore, a methodology with a mild and metal-free reaction process is highly desirable. Recently, Wang *et al.* reported the synthesis of spiro dihydrofuran derivatives through iodine-mediated reaction of aldehydes with 5,5-dimethylcyclohexane-1,3-dione [6]. Still, general and efficient methods for the synthesis of 2-spirosubstituted dihydrofuran from simple and readily available precursors are of great value.

On the other hand, zwitterionic iodonium compounds, a major class of polyvalent iodine compounds, are attractive and versatile reagents in organic synthesis [7]. Among them, phenyliodonium ylides, derived from β-dicarbonyl compounds, constitute an interesting type of hypervalent iodine compounds [8,9]. Because of their cheap and ready availability, phenyliodonium ylides have been used extensively in organic synthesis for a long time. To further expand the application of iodonium ylide-based domino reaction, in this article, we would like to report the challenging annulation of aromatic aldehydes **2** with dimidone **1** and its phenyliodonium ylide **3** leading to multifunctionalized spiro dihydrofuran derivatives (Scheme 1). The great aspect of the present domino reaction is shown by the fact that the formation of 2-spirosubstituted dihydrofuran skeleton and its spiro-substitution were readily achieved via iodonium ylide-based reaction in an intermolecular manner and in a one-pot operation.

RESULTS AND DISCUSSION

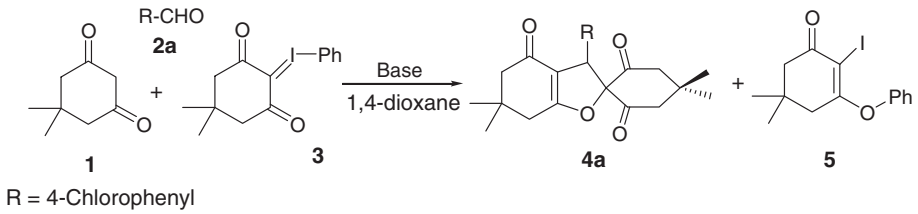
To optimize the reaction conditions for the formation of the target compounds, we started this study by treating 4-chlorobenzaldehyde **2a** and dimidone **1** with idonium ylides **3** in a ratio of 1:1:1.1 using various bases in 1, 4-dioxane, such as $NaHCO_3$, K_2CO_3, Et_3N, piperidine, and *N,N*-dimethyl- 4-aminopyridine (DMAP) under microwave (MW) irradiation. Only a trace amount of **4a** was observed when $NaHCO_3$ and K_2CO_3 were employed. Other organic bases including Et_3N, piperidine, and DMAP facilitated the reaction to some extent, but 2-iodo-5, 5-dimethyl-3-phenoxycyclohex-2- enone **5** as the main product was also isolated. It is well-known that the phenyliodonium ylide **3** easily underwent rearrangement to give the 2-iodo-5,5-dimethyl-3-phenoxycyclohex-2-enone

Scheme 1. Reaction of aldehydes with dimidone and its phenylidonium ylide.



(Scheme 2) (Fig. 1). Thus, there is the urgent demand to search the appropriate conditions including bases and solvents to decease the yield of byproduct **5**. Luckily, KOH as a base resulted in a desired 2-spirosubstituted dihydrofurans **4a** as main product. The reaction media were then examined carefully (Table 1, entries 1–6). 1,4-dioxane as a solvent can provide the spiro[benzofuran-2(4H), 1′-cyclohexane] derivatives in 45% chemical yield. Other solvents, such as *N,N*-dimethylformamide (DMF), ethane-1, 2- diol and methanol, resulted in spiro[benzofuran-2(4H), 1′-cyclo- hexane] derivatives in poor yields. This outcome was also found in the case of solvent-free conditions. To further optimize reaction conditions, the reaction was performed in 1,4-dioxane and repeated many times at different temperatures and the amount of bases in a sealed vessel under microwave irradiation. The yield of product **4a** was increased from 69 to 81% as the temperature varied from 80 to 110°C (Table 1, entries 6–8). Further increase of reaction temperature failed to improve the yield of product **4a** (Table 1, entry 9)

With the optimized conditions in hand, the scope and generality of the reaction were explored. A variety of substituents of different electronic properties reacted smoothly and efficiently under the present conditions, affording the corresponding spiro dihydrofuran products in good yields. The aromatic aldehydes with an electron-donating group exhibited less reactivity than that bearing an electron-withdrawing group (Table 2, entries 1–12).



Scheme 2

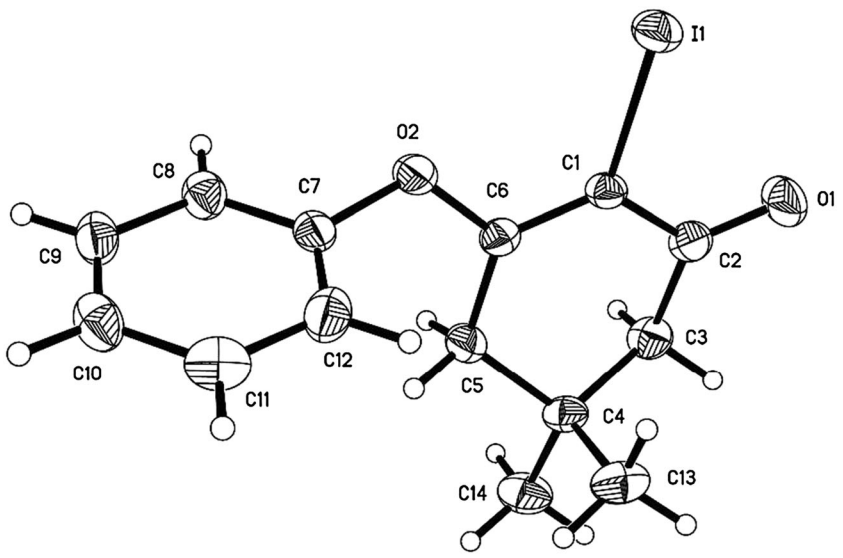


Figure 1. X-ray crystallography structure of compound **5**.

Table 1

Optimized conditions for **4a** under MW.

Entry	Solvent	KOH (equiv)	T (°C)	Time (min)	Yield (%)
1	CH_3OH	0.5	80	15	20
2	DMF	0.5	80	15	28
3	Ethane-1,2-diol	0.5	80	15	35
4	Solvent-free	0.5	80	15	32
5	1,4-Dioxane	0.5	80	15	45
6	1,4-Dioxane	1.0	80	15	69
7	1,4-Dioxane	1.0	100	12	74
8	1,4-Dioxane	1.0	110	12	81
9	1,4-Dioxane	1.0	120	12	78

Table 2

Synthesis of 2-spirosubstituted dihydrofurans **4**.

Entry	R	**4**	Time (min)	Yield (%)
1	4-Chlorophenyl (**2a**)	**4a**	12	81
2	4-Fluorophenyl(**2b**)	**4b**	14	82
3	2-Chlorophenyl(**2c**)	**4c**	15	75
4	3,4-Dichlorophenyl(**2d**)	**4d**	12	83
5	4-Tolyl(**2e**)	**4e**	18	82
6	4-Methoxyphenyl(**2f**)	**4f**	18	81
7	3,4-Dimethyphenyl(**2g**)	**4g**	20	80
8	3,4-Dimethoxyphenyl(**2h**)	**4h**	20	81
9	3,4,5-Trimethoxyphenyl(**2i**)	**4i**	20	76
10	4-Nitrophenyl(**2j**)	**4j**	12	86
11	3-Nitrophenyl(**2k**)	**4k**	12	85
12	4-Cyanophenyl(**2l**)	**4l**	13	80
13	Pyridin-2-yl(**2m**)	**4m**	16	68
14	Thiophen-2-yl(**2n**)	**4n**	18	82
15	Furan-2-yl(**2o**)	**4o**	18	70
16	Ethyl(**2p**)	**4p**	20	72
17	Propyl(**2q**)	**4q**	24	75
18	Isobutyl(**2r**)	**4r**	25	79

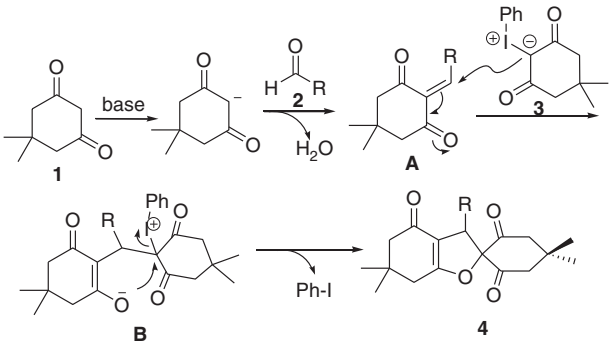
The reaction time was prolonged to 18–20 min, and the corresponding products were obtained in good yields as well. And then, the heteroaromatic aldehydes, such as 2-pyridinecarboxaldehyde, 2-thiophenecarboxaldehyde, and 2-furancarboxaldehyde, were also tolerated under the current conditions, furnishing the spiro dihydrofuran products in 68–82% yields (Table 2, entries 13–15). Furthermore, aliphatic aldehydes such as propionic aldehyde, butyraldehyde, and 3-methyl butyraldehyde were also investigated. Smooth reactions were observed for these aldehydes and delivered the final products in 70–79% yields (Table 2, entries 16–18). When cyclohexane-1,3-dione was further investigated, unfortunately, the spiro dihydrofuran products failed to obtain, and the complex mixtures were generated. The reason is not clear so far. Moreover, functional groups like bromide and chloride were well tolerated. These functional groups provide ample opportunity for further functional group manipulations, for example, by modern cross-coupling reactions. It is worthy to note that only microwave irradiation can make the present multi-component domino reaction to occur rapidly and efficiently, whereas normal heating diminished both yield and speed [10–12].

The mechanism of this domino reaction is proposed in Scheme 3. An initial condensation generated intermediate A, which successively underwent intermolecular Michael addition (A to B) and nucleophilic substitution (B to 4) to give final products **4**. In the reaction, the iodonium ylide first acted as a nucleophile and followed to convert into the electrophilic reagent.

All new products were fully characterized by spectroscopic analyses, and the IR, 1H NMR, HRMS data were consistent with their structures (for the spectra of all pure products, see the ESI). Furthermore, crystal of **4e** was obtained by careful recrystallization from a co-solvent of DMF and ethanol, and its structure was unambiguously confirmed by X-ray crystallography (Fig. 2) [13].

Besides a high efficiency in the formation of multiple bonds as a domino process, this reaction has the following advantages: (1) the starting materials are readily available, and the reagents are very cheap; (2) the convenient work-

Scheme 3. The reasonable mechanism for the formations of 2-spirosubstituted dihydrofurans **4**.



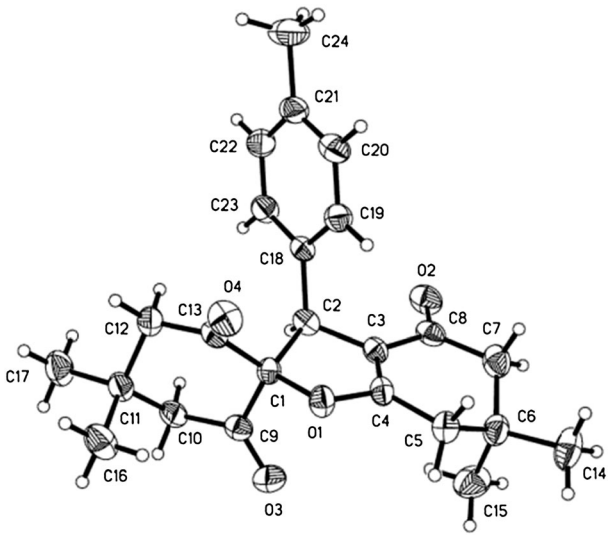


Figure 2. X-ray crystallography structure of compound **4e**.

up which only needs simple filtration because the products directly precipitate out after the reaction system is neutralized with acid and when its mixtures are diluted with cold water. (3) This method requires a short reaction time; (4) the regiospecific construction of 2-spirosubstituted dihydrofuran skeleton. The novelty of the present three-component domino reaction is shown by the fact that multiple chemical bonds' breaking and forming were simultaneously achieved in an intermolecular manner.

In summary, we have described iodonium ylide-based three-component heterocyclization reactions (aldehydes, dimidone, and its phenylidonium ylide) as an alternative method for efficient synthesis of 2-spirosubstitued dihydrofurans under microwave irradiation. This methodology is simple, practical, which is a regioselective and alternative synthetic route to obtain good yields of 2-spirosubstituted dihydrofuran derivatives. This method is much more efficient because of short reaction times and easy work-up.

EXPERIMENTAL

Microwave irradiation was carried out with Initiator from Biotage Company, Uppsala, Sweden. Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on an FT-IR-tensor 27 spectrometer. ^{1}H NMR spectra were measured on a DPX 400 MHz spectrometer (Bruker Company, Ettlingen, Germany) using TMS as an internal standard and DMSO-d_6 as solvent. HRMS (ESI) was determined by using the micrOTOF-Q II HPLC/MS instrument (Bruker Company, Ettlingen, Germany). X-Ray crystallographic analysis was performed with a Siemens SMART CCD and a Siemens P4 diffractometer (Siemens Company, München, Germany).

Procedure for the synthesis of phenyliodonium ylide 3 [14]:. To a solution of cyclic the dimedone **1** (20 mmol) in 30 mL methanol, 10% KOH aqueous (20 mL) was added at room temperature, and followed by addition of a solution of diacetoxy iodobenzene (21 mmol) in 40 mL methanol. The reaction mixture was stirred for 2 h at room temperature and then quenched with ice cold water. The resulting white precipitate was filtered, and mother liquor was extracted with dichloromethane, then washed with water, dried over anhydrous sodium sulfate, filtered and concentrated in vaccuo. The resultant white solid was mixed with the first crop and the mixture recrystallized from DCM/Hexanes.

General procedure for the synthesis of 2-spirosubstituted fused dihydrofurans 4 under microwave irradiation:. In a 10-mL reaction vial, aromatic aldehyde **1** (1 mmol), dimidone **2** (1 mmol), iodonium ylide **3** (1.1 mmol), KOH (1.0 mmol), and 1,4-dioxane (1.5 mL) were mixed, capped and then stirred at room temperature for 15 min. The mixture was irradiated for a given time at 110°C. Upon completion as shown by TLC monitoring, the reaction mixture was cooled to room temperature and neutralized by protonic acids and then diluted with cold water. The solid product was filtered, washed with water and acetone, and subsequently dried and then recrystallized from 80% EtOH to give the pure product.

3-(4-chlorophenyl)-4',4',6,6-tetramethyl-6,7-dihydro-3H-spiro [benzofuran-2,1'-cyclohexane]-2',4,6'(5H)-trione (4a). White solid, mp: 265–266°CIR (KBr, ν, cm^{-1}): 2959, 2929, 2873, 1740, 1713, 1650, 1531, 1384, 1353, 1234, 1204, 1164, 1099, 1046, 730, 688, 613, 555.^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.39 (d, J = 8.4 Hz, 2H, ArH), 7.28 (d, J = 8.4 Hz, 2H, ArH), 4.82(s, 1H, CH), 3.66 (d, J = 15.2 Hz, 1H, CH_2), 2.73-2.55 (m, 2H, CH_2), 2.44-2.40 (m, 1H, CH_2), 2.16-2.09 (m, 4H, CH_2), 1.08-1.07 (m, 9H, CH_3), 0.69 (S, 3H, CH_3).^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm): 199.0, 198.7, 193.6, 176.8, 134.7, 134.6, 129.8, 129.3, 113.6, 103.5, 54.2, 53.9, 51.0, 50.0, 37.3, 34.3, 30.6, 30.5, 28.9, 28.4, 26.3.HRMS (ESI) m/z: calc. for $C_{23}H_{25}ClO_4$: 423.1334 [M + Na]$^+$; found: 423.1311.

3-(4-fluorophenyl)-4',4',6,6-tetramethyl-6,7-dihydro-3H-spiro[benzofuran-2,1'-cyclohexane]-2',4,6'(5H)-trione (4b). White solid, mp: 236–237°CIR (KBr, ν, cm−1): 2962, 2928, 2873, 1747, 1718, 1644, 1468, 1390, 1193, 1138, 1039, 892, 839, 674, 614.^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.31-7.24 (m, 4H, ArH), 4.78(s, 1H, CH), 3.65 (d, J = 14.8 Hz, 1H, CH_2), 2.65 (dd, J1 = 17.6 Hz, J2 = 30.4 Hz, 2H, CH_2), 2.43 (d, J = 14.8 Hz, 1H, CH_2), 2.12-2.06 (m, 4H, CH_2), 1.10 (s, 3H, CH_3), 1.08 (s, 6H, CH_3), 0.68 (s, 3H, CH_3).^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm): 199.1, 198.8, 193.2, 176.7, 162.7 (^1J CF = 248.1 Hz), 131.9 (^4J = 3.3 Hz), 130.2 (^3J = 8.3 Hz), 116.0 (^2J = 21.7 Hz), 113.7, 103.5, 54.2, 53.9, 51.1, 50.0, 37.3, 34.3, 30.6, 30.5, 28.9, 28.4, 26.3.HRMS (ESI) m/z: calc. for $C_{23}H_{25}FO_4$: 407.1635 [M + Na]$^+$; found: 407.1638.

3-(2-chlorophenyl)-4',4',6,6-tetramethyl-6,7-dihydro-3H-spiro[benzofuran-2,1'-cyclohexane]-2',4,6'(5H)-trione (4c). White solid, mp: 253–254°CIR (KBr, ν, cm^{-1}): 2961, 2925, 2873, 1744, 1712, 1644, 1461, 1390, 1193, 1138, 1031, 892, 838, 674, 614.^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.31 (d, J = 8.4 Hz, 1H, ArH), 7.09 (d, J = 6.0 Hz, 2H, ArH), 6.93 (s, 1H, ArH), 4.56 (s, 1H, CH), 3.12 (s, 1H, CH_2), 2.65 (d, J = 12.8 Hz, 1H, CH_2), 2.36 (d, J = 12.0 Hz, 1H, CH_2), 2.25 (d. 2H, CH_2)2.12 (d, J = 9.6 Hz, 1H, CH_2), 2.05-2.06 (m, 2H, CH_2), 1.03 (s, 3H, CH_3), 0.99 (s, 3H, CH_3), 0.94 (s, 3H, CH_3),0.85 (s, 3H, CH_3).HRMS (ESI) m/z: calc. for $C_{23}H_{25}ClO_4$: 423.1334 $[M+Na]^+$; found: 423.1311.

3-(3,4-Dichlorophenyl)-4',4',6,6-tetramethyl-3,5,6,7-tetrahydro-spiro[benzofuran-2(4H),1'-cyclohexane]-2',4,6'-trione (4d). Known compoundmp 253–254 °C (lit. mp 251–252°C) [6]

4',4',6,6-tetramethyl-3-(p-tolyl)-6,7-dihydro-3H-spiro[benzofuran-2,1'-cyclohexane]-2',4,6'(5H)-trione (4e). White solid, mp: 248–249°CIR (KBr, ν, cm^{-1}): 2959, 2871, 1740, 1712, 1640, 1512, 1393, 1243, 1180, 1043, 839, 673, 547;^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.12 (d, J = 3.6 Hz, 4H, ArH), 4.73 (s, 1H, CH), 3.63 (d, J = 15.2 Hz, 1H, CH_2), 2.65 (dd, J1 = 17.6 Hz, J2 = 28.4 Hz, 2H, CH_2), 2.41 (d, J = 15.2 Hz, 1H, CH_2), 2.26 (s, 3H, CH_3), 2.15-2.04 (m, 2H, CH_2), 1.09 (s, 3H, CH_3), 1.08 (s, 6H, CH_3), 0.68 (s, 3H, CH_3).^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm): 199.4, 199.0, 193.2, 176.5, 138.4, 133.0, 129.7, 128.4, 113.7, 103.9, 54.8, 53.8, 51.1, 50.0, 37.3, 34.2, 30.5, 30.5, 28.9, 28.4, 26.3, 21.2.HRMS (ESI) m/z: calc. for $C_{24}H_{28}O_4$: 403.1885 $[M+Na]^+$; found: 403.1884.

3-(4-Methoxyphenyl)-4',4',6,6-tetramethyl-3,5,6,7-tetrahydro-spiro[benzofuran-2(4H),1'-cyclohexane]-2',4,6'-trione (4f). Known compoundmp 234–235°C (lit. mp 230–231°C) [6]

3-(3,4-Dimethylphenyl)-4',4',6,6-tetramethyl-3,5,6,7-tetrahydro-spiro[benzofuran-2(4H),1'-cyclohexane]-2',4,6'-trione (4g). Known compoundmp 245–246°C (lit. mp 242–243°C) [6]

3-(3,4-Dimethoxyphenyl)-4',4',6,6-tetramethyl-3,5,6,7-tetrahydro-spiro[benzofuran-2(4H),1'-cyclohexane]-2',4,6'-trione (4h). Known compoundmp 194–196°C (lit. mp 194–196°C) [6]

4',4',6,6-tetramethyl-3-(3,4,5-trimethoxyphenyl)-6,7-dihydro-3H-spiro[benzofuran-2,1'-cyclohexane]-2',4,6'(5H)-trione (4i). White solid, mp: 224–225°CIR (KBr, ν, cm^{-1}): 2951, 2923, 2873, 1725, 1711, 1650, 1533, 1384, 1353, 1234, 1208, 1169, 1099, 1046, 731, 688, 623, 559.^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.55 (s, 2H, ArH), 4.69 (s, 1H, CH), 3.71 (s, 6H, OCH_3), 3.63 (s, 3H, OCH_3), 2.65 (dd, J1 = 18.0 Hz, J2 = 16.8 Hz, 2H, CH_2), 2.42 (d, J = 15.2 Hz, 1H, CH), 2. 20–2.09 (m, 5H, CH_2), 1.11 (s, 3H, CH_3), 1.08 (s, 6H, CH_3), 0.69 (s, 3H, CH_3).^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm): 199.2, 199.1, 193.3, 176.6, 153.5, 131.8, 113.4, 105.7, 103.9, 60.9, 56.2, 55.6, 53.6, 51.1, 50.1, 37.3, 34.3, 30.6, 30.6, 29.1, 28.0, 26.3.HRMS (ESI) m/z: calc. for $C_{26}H_{32}O_7$: 479.2046 $[M+Na]^+$; found: 479.2026.

4',4',6,6-Tetramethyl-3-(4-nitrophenyl)-3,5,6,7-tetrahydro-spiro[benzofuran-2(4H),1'-cyclohexane]-2',4,6'-trione (4j). Known compoundmp 266–267°C (lit. mp 265–266°C) [6]

4',4',6,6-Tetramethyl-3-(3-nitrophenyl)-3,5,6,7-tetrahydro-spiro[benzofuran-2(4H),1'-cyclohexane]-2',4,6'-trione (4k). Known compoundmp 202–203°C (lit. mp 201–203°C) [6]

3-(4-Cyanophenyl)-4',4',6,6-tetramethyl-3,5,6,7-tetrahydro-spiro[benzofuran-2(4H),1'-cyclohexane]-2',4,6'-trione (4l). Known compoundmp 247–248°C (lit. mp 248–250°C)[6]

4',4',6,6-Tetramethyl-3-(pyridin-2-yl)-3,5,6,7-tetrahydro-spiro[benzofuran-2(4H),1'-cyclohexane]-2',4,6'-trione (4m). Known compoundmp 201–202°C (lit. mp 201–203°C) [6]

4',4',6,6-Tetramethyl-3-(thiophen-2-yl)-3,5,6,7-tetrahydro-spiro[benzofuran-2(4H),1'-cyclohexane]-2',4,6'-trione (4n). Known compoundmp 246–247°C (lit. mp 246–248°C) [6]

3-(Furan-2-yl)-4',4',6,6-tetramethyl-3,5,6,7-tetrahydro-spiro[benzofuran-2(4H),1'-cyclohexane]-2',4,6'-trione (4o). Known compoundmp 223–224°C (lit. mp 222–223°C) [6]

3-Ethyl-4',4',6,6-tetramethyl-3,5,6,7-tetrahydro-spiro[benzofuran-2(4H),1'-cyclohexane]-2',4,6'-trione (4p). Known compoundmp 150–152°C (lit. mp 148–149°C) [6]

4',4',6,6-Tetramethyl-3-propyl-3,5,6,7-tetrahydro-spiro[benzofuran-2(4H),1'-cyclohexane]-2',4,6'-trione (4q). Known compoundmp 165–167°C (lit. mp 168–170°C) [6]

3-isobutyl-4',4',6,6-tetramethyl-6,7-dihydro-3H-spiro[benzofuran-2,1'-cyclohexane]-2',4,6'(5H)-trione (4r). White solid, mp: 212–213°CIR (KBr, ν, cm^{-1}): 2958, 2927, 2872, 1741, 1710, 1635, 1465, 1396, 1324, 1217, 1040, 945, 727, 676, 617, 426^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.56-3.53 (m, 1H, CH), 3.48-3.44 (m, 1H, CH_2), 2.94 (d, J. = 16.0 Hz, 2H, CH_2) 2.68-2.67 (m, 1H, CH) 2.43-2.30 (m, 3H, CH_2), 2.17 (d, J = 16.0 Hz, 1H, CH_2), 2.06 (d, J = 16.0 Hz, 1H, CH_2) 1.17 (s, 3H, CH_3), 1.14-1.09 (m, 2H, CH_2), 1.04 (s, 3H, CH_3), 1.03 (s, 3H, CH_3), 0.96 (s, 3H, CH_3), 0.78 (s, 3H, CH_3), 0.72 (s, 3H, CH_3).^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm): 199.8, 199.4, 194.1, 177.4, 114.9, 103.9, 54.7, 51.3, 50.2, 45.9, 41.7, 37.4, 34.0, 30.8, 30.5, 28.6, 28.4, 25.9, 25.3, 24.0, 21.7.HRMS (ESI) m/z: calc. for $C_{21}H_{30}O_4$: 369.2042 $[M+Na]^+$; found: 369.2028.

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REFERENCES AND NOTES

[1] (a) Eicher, T.; Haputmann, S.; Suschitzky, H. Eds. In The Chemistry of Heterocycles: Structure, Reactions, Syntheses, and Applications; Wiley-VCH: Weinheim, 2003; (b) Lipshutz, B. H. Chem Rev 1986, 86, 795.

[2] Dimroth, P.; Pasedach, H. Angew Chem 1960, 22, 865.

[3] Mcdonald, F. E.; Connolly, C. B.; Gleason, M. M.; Towne, T. B.; Treiber, K. D. J Org Chem 1993, 58, 6952.

[4] (a) Pirrung, M. C.; Blume, F. J Org Chem 1999, 64, 3642; (b) Lee, Y. R.; Suk, J. Y. Tetrahedron 2002, 58, 2359; (c) Lee, Y. R.; Hwang, J. C. Eur J Org Chem 2005, 1568.

[5] (a) Hwu, J. R.; Chen, C. N.; Shiao, S.-S. J Org Chem 1995, 60, 856; (b) Nishino, H.; Nguyen, V.-H.; Yoshinaga, S.; Kurosawa, K. J Org Chem 1996, 61, 8264; (c) Garzino, F.; Meou, A.; Brun, P. Tetrahedron Lett 2000, 41, 9803; (d) Burgaz, E. V.; Yilmaz, M.; Pekel, A. T.;O Ktemer, A. Tetrahedron 2007, 63, 7229; (e) Wang, G.-W.; Dong, Y.-W.; Wu, P.; Yuan, T.-T.; Shen, Y.-B. J Org Chem 2008, 73, 7088.

[6] Wang, G.-W.; Gao, J. Org Lett 2009, 11, 2385.

[7] (a) Varvoglia, A. The Organic Chemistry of Polycoordinated Iodine; VCH: New York, 1992; (b) Spyroudis, S.; Tarantili, P. J Org Chem 1993, 58, 4885; (c) Moriarty, R. M.; Vaid, R. K. Synthesis 1990, 431; (d) Yamada, Y.; Yamamoto, T.; Okawara, M. Tetrahedron Lett 1975, 16, 361; (e) Hood, J. N. C.; Lloyd, D.; MacDonald, W. A.; Shepherd, T. M. Tetrahedron 1982, 38, 3355; (f) Margaret, B. C.; Aurora, E. C.; Tabitha, A. L.; JoAnn, P.-D. J Am Chem Soc 2000, 122, 5210; (g) Matveeva, E. D.; Podrugina, T. A.; Pavlova, A. S.; Mironov, A. V.; Borisenko, A. A.; Gleiter, R.; Zefirov, N. S. J Org Chem 2009, 74, 9428; (h) Marcoux, D.; Goudreau, S. R.; Charette, A. B. J Org Chem 2009, 74, 8939; (i) Matveeva, E. D.; Podrugina, T. A.; Pavlova, A. S.; Mironov, A. V.; Zefirov, N. S. Russ Chem Bull 2008, 57, 2237; (j) Li, H.-Y.; Hsung, R. P. Org Lett 2009, 11, 4462; (k) Matveeva, E. D.; Podrugina, T. A.; Pavlova, A. S.; Mironov, A. V.; Gleiter, R.; Zefirov, N. S. Eur J Org Chem 2009, 2323; (l) Elizabeth, M.-X.; Spyroudis, S. Synlett 2008, 2725.

[8] (a) Koser, G. F. The Chemistry of Functional Groups; Wiley: New York, 1983; (b) Macikenas, D.; Skrzypczak-Jankun, E.; Protasiewicz, J. D. J Am Chem Soc 2011, 133, 4151; (c) Matveeva, E. D.; Podrugina, T. A.; Taranova, M. A.; Borisenko, A. A.; Mironov, A. V.; Gleiter, R.; Zefirov, N. S. J Org Chem 2011, 76, 566; (d) Matveeva, E. D.; Gleiter, R.; Zefirov, N. S. Russ Chem Bull 2010, 59, 488; (e) Kefalidis, C. E.; Kanakis, A. A.; Gallos, J. K.; Tsipis, C. A. J Organomet Chem 2010, 695, 2030; (f) Moriarty, R. M.; Tyagi, S.; Kinch, M. Tetrahedron 2010, 66, 5801; (g) Glinis, E.; Malamidou-Xenikaki, E.; Skouros, H.; Spyroudis, S.; Tsanakopoulou, M. Tetrahedron 2010, 66, 5786.

[9] (a) Koser, G. F.; Yu, S. M. J Org Chem 1975, 40, 1166; (b) Papadopoulou, M.; Spyroudis, S.; Varvogliis, A. J Org Chem 1985, 50, 1509; (c) Hadjiarapoglou, L. Tetrahedron Lett 1987, 28, 4449; (d) Hatjigjigrigoriou, E.; Spyroudis, S.; Varvoglis, A. Liebigs Ann Chem 1989, 167; (e) Moriarty, R. M.; Prakash, 0.; Vaid, R. K.; Zhao, L. J Am Chem Soc 1989, 111, 6443; (f) Spyroudis, S. Liebigs Ann Chem 1986, 947; (g) Spyroudis, S. J Org Chem 1986, 51, 3453; (h) Hadjiarapoglou, L.; Spyroudis, S.; Varvoglis, A. J Am Chem Soc 1985, 107, 7178.

[10] (a) Jiang, B.; Tu, S.-J.; Parminder, K.; Walter, W.; Li, G. J Am Chem Soc 2009, 131, 11660; (b) Jiang, B.; Li, C.; Shi, F.; Tu, S.-J.; Kaur, P.; Wever, W.; Li, G. J Org Chem 2010, 75, 2962; (c) Jiang, B.; Wang, X.; Shi, F.; Tu, S.-J.; Ai, T.; Ballew, A.; Li, G. J Org Chem 2009, 74, 9486; (d) Ma, N.; Jiang, B.; Zhang, G.; Tu, S.-J.; Walter, W.; Li, G. Green Chem 2010, 12, 1357; (e) Jiang, B.; Rajale, T.; Walter, W.; Tu, S.-J.; Li, G. Chem Asian J 2010, 5, 2318.

[11] (a) Tu, S.-J.; Cao, X.-D.; Hao, W.-J.; Zhang, X.-H.; Yan, S.; Wu, S.-S.; Han, Z.-G.; Shi, F. Org Biomol Chem 2009, 7, 557; (b) Jiang, B.; Hao, W.-J.; Zhang, J.-P.; Tu, S.-J.; Shi, F. Org Biomol Chem 2009, 7, 1171; (c) Hao, W.-J.; Jiang, B.; Tu, S.-J.; Cao, X.-D.; Wu, S.-S.; Yan, S.; Zhang, X.-H.; Han, Z.-G.; Shi, F. Org Biomol Chem 2009, 7, 1410; (d) Jiang, B.; Hao, W.-J.; Zhang, J.-P.; Tu, S.-J.; Shi, F. Org Biomol Chem 2009, 7, 2195; (e) Jiang, B.; Shi, F.; Tu, S.-J. Curr Org Chem 2010, 14, 357.

[12] (a) Tu, S.; Wu, S.; Han, Z.; Hao, W. Chin J Chem 2009, 27, 1148; (b) Peng, J.; Hao,W.; Wang, X.; Tu, S.; Ma, N.; Zhang G.; Chin J Chem, 2009, 27, 1707; (c) Peng, J.; Jia, R.; Xu, Y.; Tu, S.; Ma, N.; Zhang, G. Chin J Chem, 2009, 27, 2392; (d) Wang, S.; Cheng, C.; Gong, F.; Wu, F.; Jiang, B.; Zhou, J.; Tu, S. Chin J Chem 2011, 29, 2101; (e) Wang, S.; Wang, X.; Tu, M.; Jiang, B.; Tu, S. Chin J Chem 2011, 29, 2411.

[13] The single-crystal growth was carried out in co-solvent of DMF and EtOH at room temperature. X-ray crystallographic analysis was performed with a Siemens SMART CCD and a Siemens P4 diffractometer. Crystal data for **4e**: $C_{24}H_{28}O_4$, crystal dimension $0.42 \times 0.13 \times 0.07$ mm, Monoclinic, space group P2(1)/c, a = 5.9587(7) Å, b = 17.6616(19) Å, c = 20.450(2) Å, $\alpha = \gamma = 90^o$, $\beta = 95.2390(10)^o$, V = 2143.1(4) Å ^{3}, Mr = 380.46, Z = 4, $\lambda = 0.71073$ Å, μ (Mo K_α) = 0.079 mm^{-1}, F(000) = 816, $R_1 = 0.0464$, $wR_2 = 0.0681$. Crystal data for **5**: $C_{14}H_{15}IO_2$, crystal dimension $0.42 \times 0.30 \times 0.20$ mm, Triclinic, space group P-1, a = 8.1650(8) Å, b = 9.4514(10) Å, c = 9.8500(14) Å, $\alpha = 113.797(2)^o$, $\beta = 101.1010(10)^o$, $\gamma = 94.8510(10)^o$, V = 671.26(14) Å ^{3}, Mr = 342.16, Z = 2, $\lambda = 0.71073$ Å, μ (Mo K_α) = 2.373 mm^{-1}, F(000) = 336, $R_1 = 0.0288$, $wR_2 = 0.0707$.

[14] Moriarty, R. M.; Tyagi, S.; Ivanov, D.; Constantinescu, M. J Am Chem Soc 2008, 130, 7564.